

Haemodynamic changes in patients with high pulmonary vascular resistance after mitral valve replacement

Comparative study between use of unstented aortic homograft valves and Starr-Edwards prostheses

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The clinical and haemodynamic responses to mitral valve replacement were studied in 36 patients with a pulmonary vascular resistance of 4 units or above. In 19 patients, 13 women and 6 men (mean age 49.7 years) Starr-Edwards prostheses were used. In 17 patients, 7 women and 10 men (mean age 53.6 years) fresh unstented aortic homografts were inserted. In the latter group, 3 patients had, in addition, homograft replacement of the aortic valve. Both groups showed considerable symptomatic relief after operation. Reduction in indirect mean left atrial pressure, pulmonary artery systolic and mean pressure, mean pulmonary artery - mean wedge pressure, and AV oxygen difference and pulmonary vascular resistance were observed in both groups, but with the exception of pulmonary vascular resistance and the AV oxygen difference the mean falls tended to be greater in the homograft group than in the Starr-Edwards group. However, only the fall in mean wedge pressure and the change in right atrial pressure were shown to be statistically more significant ($P < 0.05$) in the homograft group than the Starr-Edwards group. A small rise in cardiac output occurred in both groups. Pulmonary hypertension and pulmonary vascular resistance did not remain fixed as they always fell after homograft replacement of the mitral valve. The clinical and haemodynamic findings in this series suggest that patients with homograft replacement of the mitral valve have a better result than those after insertion with a Starr-Edwards prosthesis.

The rise in left atrial pressure that occurs as a consequence of mitral valve disease results in passive pulmonary hypertension because of the increased pressure needed to maintain an adequate pulmonary circulation. In some patients the pulmonary hypertension becomes further accentuated by active pulmonary vasoconstriction or by obliterative and possibly irreversible changes in the lung vessels. A simple haemodynamic means of assessing these changes in the lung vasculature is the measurement of pulmonary vascular resistance in units = (mean pulmonary artery pressure - mean left atrial pressure (mmHg)/cardiac output (l./min)). This simple concept is based on Ohm's law which is true only for

steady flows and where the resistance does not vary with the pressure difference across the circuit. Neither of these is true in the pulmonary circulation. However, despite these limitations, the measurement of pulmonary vascular resistance has proved to be useful in the assessment of patients with mitral valve disease.

Formerly patients with pronounced increase in the pulmonary vascular resistance had been thought unsuitable for operative treatment of mitral valve disease because of the high mortality and because it was believed that the pulmonary hypertension had become irreversible. In an attempt to differentiate between the reversible (vasoconstrictive) and irreversible (obliterative) elements, the injection of acetyl choline directly into the pulmonary artery has been suggested (Wood *et al.*, 1957). If the fall

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in the pulmonary artery pressure was less than 15 mmHg, it was thought that the pulmonary vascular resistance had probably become fixed (Emanuel, 1963). With improvements in surgical and perfusion techniques it is now possible to operate on patients with a very high pulmonary vascular resistance with more adequate correction of the mitral valve dysfunction than before and with acceptable mortality. This offers an opportunity to characterize more accurately the postoperative changes in the pulmonary vascular resistance in response to different operations on the mitral valve. Previous studies have shown varying degrees of relief of pulmonary hypertension after mitral valvotomy (Emanuel, 1963), mitral valve repair (Ramirez, Grimes and Abelman, 1968), or replacement using prosthetic valves (Braunwald *et al.*, 1965; Kloster *et al.*, 1969). The use of unstented aortic homografts for mitral valve replacement offers the advantage of a central unimpeded flow and does not interfere with left ventricular function (Yacoub and Kittle, 1969; Yacoub, Towers, and Somerville, 1972). The haemodynamic response of patients with pulmonary hypertension to this operation has not been reported before. The purpose of this study is to evaluate the haemodynamic changes after mitral valve replacement in patients with a raised pulmonary vascular resistance of 4 units or above and to compare the findings after homograft replacement to those after prosthetic replacement.

Patients and methods

Thirty-six consecutive patients with severe mitral valve disease with pulmonary hypertension and a pulmonary

vascular resistance of 4 units or above who survived operation at Harefield Hospital during the period September 1967 to March 1971 were studied before and after mitral valve replacement. Starr-Edwards valves were used before September 1969, after which aortic homografts were used almost exclusively for mitral valve replacement. Seventeen patients had aortic homograft replacement of the mitral valve and 19 patients had replacement with a Starr-Edwards valve prosthesis.

Of the 19 patients with the Starr-Edwards prosthesis, 14 had model 6300 and 5 had model 6120. The ages ranged from 30 to 65 years with a mean of 49.7 years. There were 13 women and 6 men. All patients had severe mixed mitral valve disease and only the mitral valve was replaced. Five patients had mild aortic incompetence detected clinically and angiographically before operation. In all patients no significant aortic regurgitation was found, on clinical examination at the time of reinvestigation. Two patients were thought to have mild tricuspid incompetence preoperatively. The mean time interval between operation and reinvestigation was 24 months, ranging from 9 months to 42 months.

In 17 patients the mitral valve was replaced by a fresh unstented aortic homograft using the techniques previously described (Yacoub and Kittle, 1969, 1970). The age varied from 28 to 66 years, with a mean of 53.6 years. There were 7 women and 10 men. All except 3 patients had severe mixed mitral valve disease. The remaining 3 had pure mitral incompetence due to ruptured chordae. In addition 3 patients had severe aortic valve disease necessitating replacement in each case with an unstented aortic homograft valve. Tricuspid incompetence of moderate severity was detected at operation in 2 patients only. The mean time from operation to reinvestigation was 9 months, ranging from 6 to 16 months, except for one patient who was reinvestigated only 3 months after operation. The interval between

TABLE I Summary of mean values of haemodynamic data studied after mitral valve replacement with paired *t*-test for significance of change within homograft and Starr-Edwards groups

Variables	Homografts (n = 17)						Starr valves		
	Preoperative		Postoperative		Mean of difference	Standard error of difference $= \sqrt{\frac{s}{n}}$	Paired <i>t</i> -test P	Preoperative	
	Mean	SD	Mean	SD				Mean	SD
Pulmonary capillary venous wedge pressure*	19.41	8.08	11.18	6.74	8.23	2.27	<0.005	18.47	5.31
Mean pulmonary artery pressure*	44.53	13.26	27.59	9.01	16.94	2.64	<0.001	42.16	13.51
Pulmonary artery systolic pressure*	72.24	25.67	43.59	13.03	28.65	5.20	<0.001	63.68	22.74
Mean right atrial pressure*	2.53	3.80	1.06	3.23	1.47	0.94	>0.1	3.47	3.84
Mean pulmonary artery - mean pulmonary capillary vein pressure*	25.24	9.94	16.53	7.17	8.71	1.45	<0.001	23.68	11.69
AV oxygen difference (vol. %)	64.54	10.94	58.45	13.18	6.09	3.80	>0.1	69.14	14.78
Pulmonary vascular resistance†	8.76	3.85	5.19	2.53	3.57	0.55	<0.001	9.14	5.98
Cardiac output‡	2.95	0.51	3.42	1.00	-0.47	0.26	>0.05	2.77	0.66

* mmHg.

† Arbitrary units, see text.

‡ litres/min.

operation and follow-up in the Starr valve group was significantly greater than in the homograft group.

All pressures were measured using Bell and Howell strain gauge transducers with Devices direct writing recording equipment, using the sternal angle as zero reference point. The following parameters were measured and used in the haemodynamic assessment: PCV (wedge) mean pressure, pulmonary artery systolic and mean pressure, and mean right atrial pressure. The arterial and mixed venous oxygen saturations were measured using the Kipp and Zonen Haemoreflexor, and expressed in volumes per cent using the formula: oxygen content = $\text{Hb(g)} \times 1.36 \times \% \text{ saturation}$.

The oxygen uptake per minute was calculated from the tables of Robertson and Reid (1952) using standard calorie consumption per square metre of body surface. The body surface area was calculated from the nomogram using height and weight data published by Documenta Geigy (6th ed., 1962). The cardiac output was measured by the direct Fick principle. The pulmonary vascular resistance was calculated in units according to the formula: $\text{PVR} = \text{mean PA} - \text{mean PCV (mmHg)} / \text{cardiac output (l./min)}$.

The cardiopulmonary bypass times in each group were compared in view of the different operative techniques involved in homograft and Starr-Edwards valve replacement.

The values obtained for 8 parameters of haemodynamic function studied were analysed statistically by using the paired Student t-test on the difference between individual pairs of readings taken before and after operation in both groups of patients. An unpaired t-test was used to compare the two groups of patients before and after treatment.

Results

The unpaired Student t-test on the preoperative values of the 8 haemodynamic variables studied showed no significant difference between the two groups of patients. A summary of the mean values of the pre- and postoperative haemodynamic data with statistical analysis is presented in Table 1.

($n = 19$)

Postoperative		Mean of difference	Standard error of difference	Paired t-test P
Mean	SD			
			$= \sqrt{\frac{s}{n}}$	
16.94	7.11	1.53	2.19	>0.4
32.74	12.53	9.42	4.31	<0.05
52.00	19.00	11.68	6.58	>0.05
5.82	5.28	-2.35	1.45	>0.1
15.79	7.95	7.89	3.14	<0.05
59.02	16.20	10.12	4.81	<0.05
4.96	2.33	4.18	1.49	<0.02
3.31	0.89	-0.54	0.27	>0.05

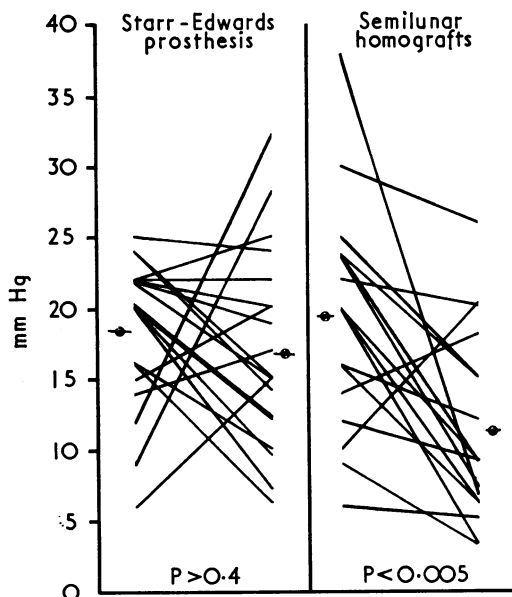


FIG. 1 Changes in wedge pressure after mitral valve replacement.

Mean wedge pressures

In patients with homograft valves the mean wedge pressure fell from 19.4 mmHg before operation to 11.2 mmHg after operation, representing a mean fall of 8.2 mmHg (Fig. 1). This was statistically significant ($P < 0.005$). In all patients except 2 there was a fall of wedge pressure. In the Starr valve group the mean wedge pressure fell from 18.5 mmHg before operation to 16.9 mmHg after operation, representing a mean fall of 1.6 mmHg (Fig. 1). This was not statistically significant ($P > 0.4$). Six of the 19 patients showed a rise in mean wedge pressure after operation, and in one patient the wedge pressure was unchanged.

Mean pulmonary artery pressure

In the homograft group the mean pulmonary artery pressure fell from 44.5 mmHg to 27.6 mmHg, representing a mean fall of 16.9 mmHg (Fig. 2). This was highly significant ($P < 0.001$). All patients showed a fall in mean pulmonary artery pressure.

In the Starr valve group the pulmonary artery pressure fell from 42.2 mmHg to 32.7 mmHg representing a fall of 9.5 mmHg (Fig. 2). This was statistically significant ($P < 0.05$). Seven patients in this group showed a rise in the pulmonary artery pressure after operation.

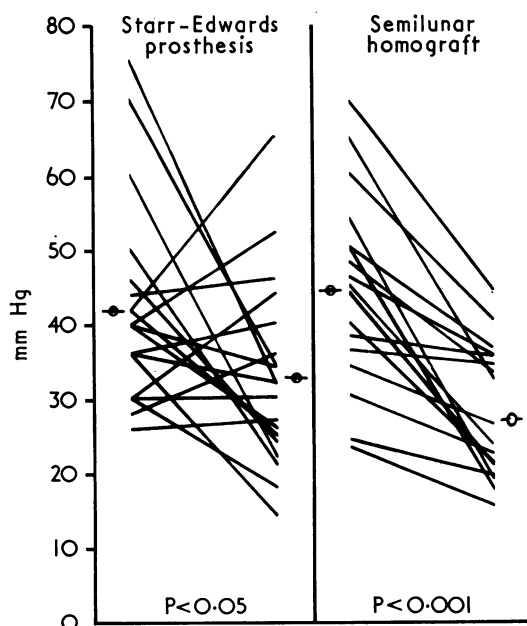


FIG. 2 Changes in pulmonary arterial mean pressure after mitral valve replacement.

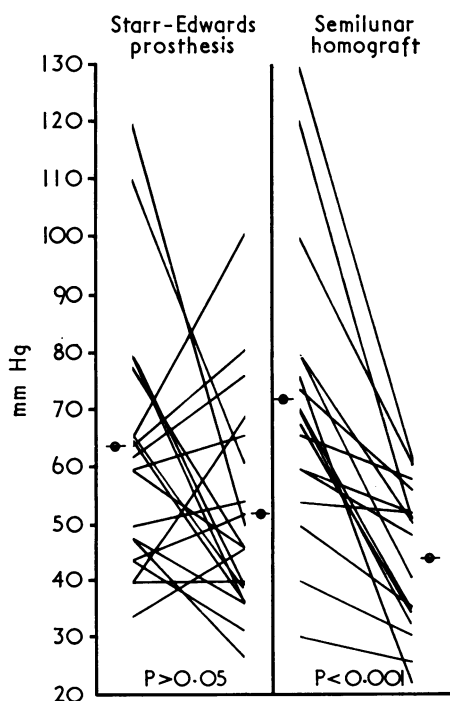


FIG. 3 Changes in pulmonary arterial systolic pressure after mitral valve replacement.

Pulmonary artery systolic pressure

After homograft valve replacement the mean pulmonary artery systolic pressure fell from 72.2 mmHg to 43.6 mmHg, representing a mean fall of 28.6 mmHg (Fig. 3). This was highly significant ($P < 0.001$). All patients showed a fall in pulmonary artery systolic pressure.

In the Starr valve group the mean pulmonary artery systolic pressure fell from 63.7 mmHg to 52.0 mmHg, representing a fall of 11.7 mmHg (Fig. 3). This fall was not statistically significant ($P > 0.05$). Seven patients showed a rise in pulmonary artery systolic pressure after operation.

Mean right atrial pressure

In the homograft group the mean right atrial pressure fell from 2.5 mmHg to 1.1 mmHg (Fig. 4) representing a mean fall of 1.4 mmHg, whereas the mean right atrial pressure in the Starr valve group rose from 3.5 mmHg to 5.8 mmHg representing a mean rise of 2.3 mmHg (Fig. 4). Neither of these changes was statistically significant ($P > 0.1$).

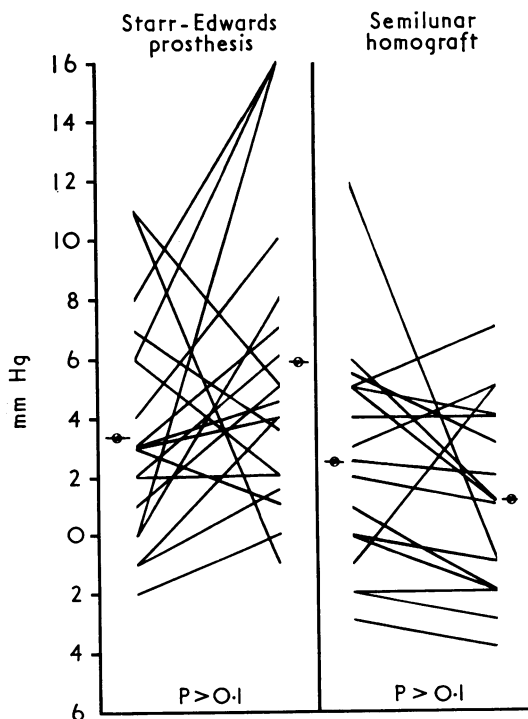


FIG. 4 Changes in mean right atrial pressure after mitral valve replacement.

Fall in pressure across pulmonary circuit (pulmonary artery – wedge mean)

In the homograft group the fall in pressure across the pulmonary circuit was 25.2 mmHg to 16.5 mmHg, representing a mean fall of 8.7 mmHg (Fig. 5). This was highly significant ($P < 0.001$). All patients showed a fall in pressure.

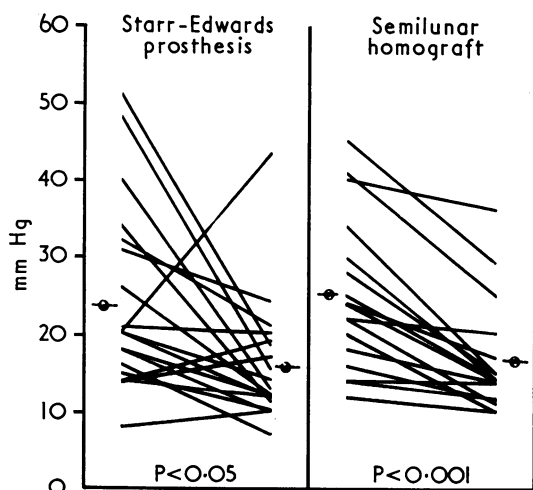


FIG. 5 Changes in (pulmonary arterial mean – mean wedge) pressure after mitral valve replacement.

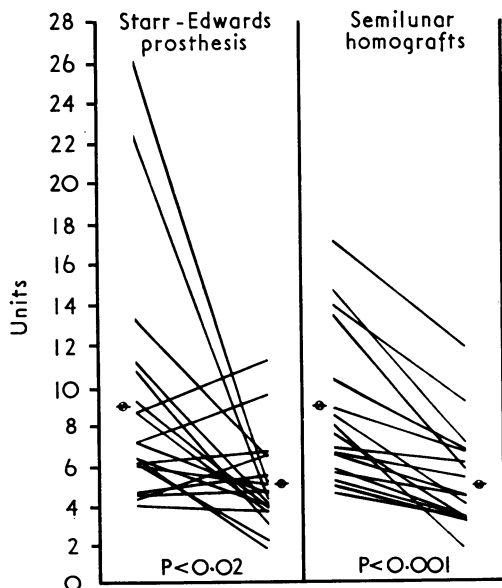


FIG. 6 Changes in pulmonary vascular resistance after mitral valve replacement.

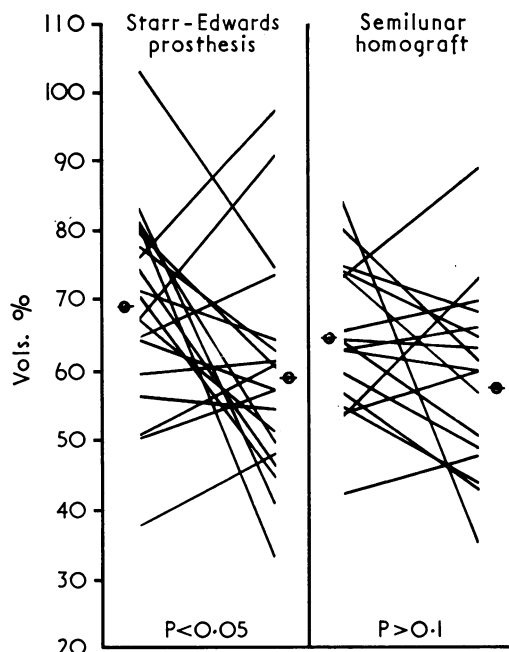


FIG. 7 Changes in arteriovenous oxygen difference after mitral valve replacement.

In the Starr valve group the mean fall in pressure across the pulmonary circuit was 23.7 to 15.8 mmHg, representing a mean fall of 7.9 mmHg (Fig. 5). This was statistically significant ($P > 0.05$). Four patients showed a rise after operation.

Pulmonary vascular resistance

In the homograft group the mean pulmonary vascular resistance fell from 8.8 to 5.2 units, representing a fall of 3.6 units (Fig. 6). This was statistically highly significant ($P < 0.001$). All patients in this group showed a fall.

In the Starr valve group the mean pulmonary vascular resistance fell from 9.1 to 5.0 units, representing a mean fall of 4.1 units (Fig. 6). This was also a statistically significant fall ($P < 0.02$). Six patients showed a small rise in the pulmonary vascular resistance after operation.

Arteriovenous oxygen difference (vol. per cent)

There was a similar fall in arteriovenous oxygen difference in both groups of patients after operation (Fig. 7), which was significant in the Starr valve group ($P < 0.05$) but did not reach significance in the homograft group ($P > 0.1$).

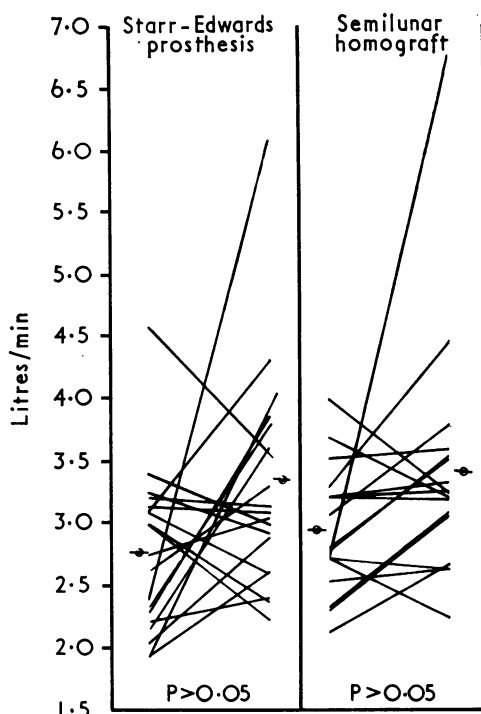


FIG. 8 Changes in cardiac output after mitral valve replacement.

Cardiac output

The mean rise in cardiac output was small in both homograft and Starr valve groups, and was 0.47 l./min and 0.54 l./min, respectively (Fig. 8). The rise was not significant either in the Starr valve group ($P > 0.05$) or in the homograft group ($P > 0.05$).

Haemodynamic data between group differences

An unpaired Student *t*-test on the significance of between group differences of the homograft and Starr-Edwards patients before and after operation is presented in Table 2. Of the 8 variables compared in this way only the difference in the fall in the wedge pressure and the change in mean right atrial pressure reached statistical significance ($P < 0.05$), while the difference in the fall in pulmonary arterial systolic pressure just failed to reach significance ($0.1 > P > 0.05$).

Discussion

This study has shown a consistent reduction in the indirect mean left atrial pressure after homograft replacement, but only an insignificant fall after Starr-Edwards prosthetic valve replacement. The average postoperative wedge pressure in the Starr-Edwards group was 16.9 mmHg which is similar to that reported using model 6300 Starr-Edwards prosthesis (Kloster *et al.*, 1969). The pressure gradient across the aortic homograft in the mitral position is usually negligible with the current technique (Yacoub *et al.*, 1972), whereas with the Starr-Edwards prosthesis model 6300, a mean resting gradient of 9.4 mmHg has been reported (Kloster *et al.*, 1969) and with model 6120 resting gradients of 4.5 mmHg (Morrow *et al.*, 1967) and 6.0 mmHg (Hodam *et al.*, 1970) have been described. On exercise these gradients would be expected to show an increase.

The average difference in mean wedge pressure in the homograft group was about 6 mmHg less than that found in the prosthetic valve group, which

TABLE 2 Unpaired student *t*-test on changes for significance of between group differences of homografts and Starr-Edwards valve before and after operation

Variables	Mean change after homograft ($n_1 = 17$)	Mean change after Starr valve ($n_2 = 19$)	Difference between homograft and Starr	SE diff. $= S \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}$	Unpaired <i>t</i> -test P
Pulmonary capillary venous wedge	8.23	1.53	6.70	3.21	< 0.05
Mean pulmonary artery pressure	16.94	9.42	7.52	5.28	> 0.1
Pulmonary artery systolic pressure	28.65	11.68	16.97	8.66	> 0.05
Mean right atrial pressure	1.47	-2.35	3.82	1.80	< 0.05
Mean pulmonary artery - mean pulmonary capillary vein pressure	8.71	7.89	0.82	3.65	> 0.8
AV O_2 difference (vol. %)	6.09	10.12	-4.03	6.33	> 0.5
Pulmonary vascular resistance	3.57	4.18	-0.61	1.69	> 0.7
Cardiac output	-0.47	-0.54	0.07	0.38	> 0.8

Except for the values for wedge pressure and mean right atrial pressure ($P < 0.05$) there is no significant difference in these variables

probably reflects the actual difference in gradients across the two different types of valve substitutes. This is further supported by the fact that 14 of the 19 patients were given model 6300, a valve which has a relatively high resting gradient across it when used in the mitral position (Kloster *et al.*, 1969). It is noteworthy that 6 patients showed a rise in wedge pressure after operation in the Starr-Edwards group, and in one patient the wedge pressure was unchanged whereas only 2 patients showed a rise in wedge pressure after operation in the homograft group. It may be that in some patients the insertion of a rigid prosthetic plastic valve which projects into the left ventricle might impair ventricular function.

Little is known of the time after operation at which the fall in left atrial pressure is maximal and for how long it continues. A fall in left atrial pressure in the immediate postoperative period following the use of discoid prosthetic valves has been reported (Dalen *et al.*, 1967) and we have found a similar fall following the use of homograft valves. In contrast, Rastelli and Kirklin (1966) observed a high left atrial pressure in the immediate postoperative period after Starr-Edwards prosthetic replacement of the mitral valve, which did not change within the three days of postoperative assessment. The early and relatively large reduction in left atrial pressure which occurred in the homograft group suggests that with the further passage of time, providing the valve remains competent, a further fall in left atrial pressure could be expected.

Both groups showed similar and statistically significant falls after operation in pulmonary vascular resistance, pulmonary artery mean pressure and reduction in pressure across the pulmonary circuit, whereas the fall in mean wedge pressure and pulmonary artery systolic was only significant in the homograft group. Of these five haemodynamic variables the mean fall was greatest after operation in the homograft group except in the case of the pulmonary vascular resistance the fall in which was slightly greater in the Starr-Edwards group. However, these differences in the falls in mean values failed to reach statistical significance except the fall in wedge pressure and right atrial pressure after operation which were greater in the homograft group than in the Starr-Edwards group $P < 0.05$ (Table 2), while the corresponding falls in pulmonary artery systolic pressure just failed to reach significance ($P > 0.05$). Thus in the majority of patients in the Starr-Edwards valve group (15 out of 19) there was a rise in right atrial pressure after operation; whereas the reverse was true in the homograft group in which 14 patients out of 17 showed a fall. In the Starr-Edwards group this rise in right atrial pressure could be due to right

ventricular dysfunction secondary to residual pulmonary hypertension or to the development of tricuspid regurgitation. However, only two patients in the latter group presented a full clinical criteria to make a diagnosis of mild to moderate tricuspid regurgitation. No patient with homograft valve replacement developed detectable tricuspid regurgitation.

The mean reduction in pulmonary vascular resistance was similar in both groups. In both groups those patients with the largest rise in pulmonary artery pressure and pulmonary vascular resistance before operation showed the largest fall in these values after operation. In the majority of patients the pulmonary vascular resistance did not return to normal. An increase in pulmonary vascular resistance may result from a fall in cardiac output and/or an increase in the value of (pulmonary arterial mean - mean wedge pressure). Of the 6 patients who showed a rise in pulmonary vascular resistance in the Starr-Edwards group, 3 patients had both a reduction in cardiac output and an increase in the calculated (pulmonary artery mean - wedge mean) pressure value, whereas 2 patients showed a reduction in cardiac output only, and 1 patient showed an increase in (pulmonary artery mean - wedge mean) pressure only. The rise in left atrial pressure and the consequent rise in pulmonary vascular resistance may be due to several factors (Peterson *et al.*, 1967). These include the presence of other significant valve disease, myocardial factors, other associated medical disease, a prolonged bypass time, possible malfunction of the Starr-Edwards prosthesis, and the model of the prosthesis used. Of these 6 patients with adverse haemodynamic results no patient had preoperative evidence of serious involvement of either aortic or tricuspid valve. This was confirmed clinically at the time of reinvestigation. These patients may have had progressive rheumatic myocarditis, but if this was so similar deterioration of some patients in the homograft group might have been expected. However, the follow-up period in the latter group is significantly less than that of the Starr valve group. There was no significant associated medical disease in these patients that might have led to the progressive deterioration of the haemodynamic state. There was no significant difference in the mean cardiopulmonary bypass time between the homograft group (100 minutes) and the Starr-Edwards group (104 minutes). In the latter group in those 6 patients with a poor haemodynamic result the mean bypass time was 107 minutes, and in those patients with a satisfactory haemodynamic result it was 96 minutes. This factor, therefore, cannot be of major importance. On clinical examination at reinvestigation and

on screening, the prosthetic valve appeared to be functioning normally. Without angiographic studies minor leakage around the seat of the prosthesis could, however, not be excluded (Morrow *et al.*, 1967; Peterson *et al.*, 1967).

The fact that 100 per cent of patients after homograft valve replacement showed some reduction in pulmonary valve resistance challenges the previously held view that the changes that occur in pulmonary vasculature in patients with a high pulmonary vascular resistance are irreversible, and we have found that the patients with the highest pulmonary vascular resistance before operation in both groups tended to show the greatest fall after operation. This is in keeping with the findings of Braunwald *et al.* (1965). The greater fall in wedge pressure found in this series after homograft replacement of the mitral valve than that found after Starr-Edwards valve replacement is probably the result of the central non-turbulent unimpeded flow which the homograft valve offers, and is in keeping with the findings of other investigators, which suggests that after mitral valvotomy the more complete the relief of stenosis the more likely it is that the pulmonary vascular resistance will return towards normal.

It has been suggested that a rise in the left atrial pressure was the most significant factor in the pathogenesis of pulmonary vascular disease in patients with severe mitral valve disease (Wood *et al.*, 1957). Our findings, that reduction in left atrial pressure after operation is followed by a fall in pulmonary vascular resistance, support this view. It can be concluded that the extent of the reduction in left atrial pressure is the most important factor in producing a fall in pulmonary vascular resistance and that the threat of irreversible pulmonary vascular changes does not seem to be as serious in patients with mitral valve disease as it is in those with congenital heart disease, and therefore a very high pulmonary vascular resistance should not itself be a contraindication to operation.

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